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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/390,846	09/14/1999	JACOBUS JOHANNES KOK	I/95150-US/D	7646

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EXAMINER	
MINNIFIELD, NITA M	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 09/08/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/390,846	KOK ET AL.	
	Examiner	Art Unit	
	N. M. Minnifield	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,11,13,16-21,23,24 and 26* is/are pending in the application.

4a) Of the above claim(s) *15,21 and 25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,11,13,16-20,23,24 and 26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *15,21 and 25* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 08/676,882.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892) 2 sheets

2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.

4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.

5) ☐ Notice of Informal Patent Application (PTO-152)

6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on July 27, 2004 has been entered.

2. Applicants' amendment filed July 29, 2004 is acknowledged and has been entered. Claims 4-10, 12, 14 and 22 have been canceled. New claim 25 has been added. Claims 1-3, 11, 13, 16-20, 23, 24 and 26 are now pending in the present application. All rejections have been withdrawn in view of Applicants' amendment and/or comments with the exception of those discussed below.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). The certified copy has been filed in parent Application No. 08/676882, filed on July 3, 1996. EP Application No. 95201801.8 filed July3, 1995 is in the parent application.

5. This application contains claims 15, 21 and 25 drawn to an invention nonelected with traverse in Paper No. 3. A complete reply to the final rejection

must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

6. Claims 1-3, 11, 13, 15, 16, 18-20, 23 and 24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 1-3, 11, 13, 15, 16, 18-20, 23 and 24 are vague and indefinite because it contains the use of an alternative expression wherein the limitation covers two different elements, i.e. "immunoreactive" is not the same as "antigenic determinants". See MPEP 706.03(d), paragraph 5. Claim 16 is vague and indefinite in the recitation of "molecular weight"; how was the molecular weight of this protein determined?

7. The rejection of claims 3, 18, 23 and 24 under 35 U.S.C. 112, first paragraph is maintained for reasons set forth in the previous office action.

The rejection was on the grounds that the specification, while being enabling for an isolated 37 kd protein from *Eimeria acervulina* consisting of the amino acid sequence set forth in SEQ ID NO: 2 and a vaccine comprising the 37 kd protein, does not reasonably provide enablement for any fragment of the isolated protein, biologically active variant or immunogenically active part sequence or variant. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are broadly drawn to an isolated protein, fragments, biological variants and equivalents of the protein for use in a vaccine composition. The specification does not enable all variants and equivalents of the claimed protein.

The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of proteins broadly encompassed by the claims and the claims broadly encompass a significant number of inoperative species. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and still retain similar activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, the problem of predicting protein structure from mere sequence data of a single protein and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein and finally what changes can be tolerated with respect thereto is extremely complex and well outside the realm of routine experimentation.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications other types and the positions within the protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining similar activity are limited in any protein and the result of such modifications is unpredictable based on the instant disclosure. One skilled in the art would expect any tolerance to modification shown for a given protein to diminish with each further and additional modification, e.g. multiple substitutions. The sequence of some proteins is highly conserved and one skilled in the art would not expect tolerance to any amino acids modification in such proteins.

The specification does not support the broad scope of the claims, which encompass all modifications and fragments because the specification does not disclose the following:

- the general tolerance to modification and extent of such tolerance;
- specific positions and regions of the sequences) which can be predictably modified and which regions are critical;
- what fragments, if any, can be made which retain the biological activity of the intact protein; and
- the specification provides essentially no guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed variant or part sequence of the protein in a manner reasonably correlated with the scope of the claims broadly including any number of variants (i.e. additions, deletions or substitutions) and active part sequence (i.e. fragments of any size). The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without such guidance, the changes which can be made in the proteins structure and still maintain activity is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See Amgen. Inc. v. Chugai Pharmaceutical Co. Ltd., 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir. 1991) at 18 USPQ2d 1026-1027 and Ex parte Forman, 230 U.S.P.Q. 546 (Bd. Pat. App. & Int. 1986). In view of all of the above it is determine that it would require undue experimentation of one of skill in the art to make and use the invention commensurate in scope with the claimed subject matter.

Applicant urges that what is claimed is one or more immunoreactive fragments which is defined by the specification, one can routinely determine fragments of a protein, biological equivalents are defined in the specification and methods for establishing LDH activity of Eimeria protein are well known in the art and cites case law in support.

It is the examiner's position that page 6, lines 12-15 do not disclose any amino acid sequence of LDH which is defined as being "immunoreactive and/or antigenic determinants", "biologically active variant"' or "an immunologically active part". What is the amino acid structure of the subsequence which meets the definition of "immunogenic determinant"' or fragment of the LDH protein? The claims are not drawn to a method of measuring LDH activity. The claims are drawn to vaccines and immunoreactive fragments of the protein. The specification describes one peptide fragment, GWXQEEVDDWQK, which is found in seq. I.D. No.2. The specification, however, appears to lack enablement for the use of this fragment in a vaccine to protect (i.e. immunizing activity) against infection and disease caused by Eimeria. It appears that applicant is inviting one to experiment to determine how to use the peptide fragment to protect against disease and additionally to determine what other fragments can be generated from LDH with the claimed immunoreactivity. This experimentation is considered undue and the rejection is therefore maintained.

This rejection is maintained for the reasons of record. Applicant's arguments filed November 25, 2003 have been fully considered but they are not persuasive. Applicants have asserted that it is not unreasonable that the specification identify and test each fragment that will retain activity of the intact

protein. Further, Applicants have asserted that it is common practice to have patents that contain compounds that have not been tested for activity, with the understanding that some experimentation would be needed.

It is noted the this rejection is maintained with regard to fragments as well as claim limitations that recite a protein that comprises amino acid sequences of SEQ ID NO: 2, a biologically active variant or immunogenically active part sequence or variant (see claims 3 and 18 for example). The specification is not enabled for fragments or biologically active variants of the fragment that provide protection against coccidiosis in poultry.

With regard to the variants, it is noted that it is **not** routine in the art to screen for positions within the protein's sequence where amino acid modifications (i.e. additions, deletions, or modifications) can be made with a reasonable expectation of success in obtaining similar activity/utility are limited in any protein and the result of such modifications is unpredictable based on the instant disclosure (see Bowie et al., Science, Vol. 247, pp 1306-1310, especially p. 1306, column 2, paragraph 2 and Kumar et al. PNAS 87: 1337-1341 February 1991. One skilled in the art would expect any tolerance to modification shown for a given protein/peptide to diminish with each further and additional modification, e.g. multiple deletions or substitutions. The sequence of some proteins/peptides is highly conserved and one skilled in the art would not expect tolerance to any amino acids modification in such proteins/peptides. The specification does not support the broad scope of the claims, which encompass a multitude of polypeptides because the specification does **not** disclose the following:

- the general tolerance to modification and extent of such tolerance;
- specific positions, which can be predictably modified;

-which regions are protective; and

- essentially no guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have **not** provided sufficient guidance to enable one skilled in the art to make and use the claimed polypeptides in manner reasonably correlated with the scope of the claims broadly including any number of deletions, additions, substitutions and fragments of any size. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without such guidance, the changes which can be made and still maintain activity/utility is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See Ex parte Forman, 230 U.S.P.Q. 546 (Bd. Pat. App. & Int. 1986).

The specification does not support the broad scope of the claims which encompass all variants/analogues of the peptide and the possibility of changing one or more amino acids to any one of 23 different amino acids because the specification does not disclose the following: the general tolerance to modification (substitution, insertion, deletion) and extent of such tolerance; specific positions and regions of the sequence(s) which can be predictably modified and which regions are critical; what variants/analogues, if any, can be made which retain the biological activity, claimed activity and immunogenicity of the intact peptides; and the specification provide essentially no guidance as to which of the essentially infinite possible choices is likely to be successful.

The specification does not support the broad scope of the claims, which encompass all fragments or variants of the fragment and still have the biological activity as well as vaccine protection against coccidiosis in poultry. Further,

Houghten et al. teach that changes/modifications (addition, substitution, deletion or inversion) of one or more amino acids in a polypeptide will alter antigenic determinants and therefore effect antibody production (p. 21) as well as antibody binding. Houghten et al. also teach that "... combined effects of multiple changes in an antigenic determinant could result in a loss of [immunological] protection." and "A protein having multiple antigenic sites, multiple point mutations, or accumulated point mutations at key residues could create a new antigen that is precipitously or progressively unrecognizable by any of the antibodies..." (p. 24). Houghten et al. teach that point mutations at one key antigen residue could eliminate the ability of an antibody to recognize this altered antigen (p. 24). It is not always possible to make the derivatives that retain immunodominant regions and immunological activity if the regions have been altered. The sequence of some proteins is highly conserved and one skilled in the art would not expect tolerance to any amino acids modification in such proteins. However, even if it were shown that some modifications could be tolerated in the claimed fragments or variants thereof, for the reasons discussed the claims would still expectedly encompass a significant number of inoperative species, which could not be distinguished without undue experimentation. See Amgen, Inc. v. Chugai Pharmaceutical Co. Ltd., 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir. 1991) at 18 USPQ2d 1026-1027 and Ex parte Forman, 230 U.S.P.Q. 546 (Bd. Pat. App. & Int. 1986).

This rejection maintained for the reasons of record. Applicant's arguments filed July 29, 2004 have been fully considered but they are not persuasive. It is noted that the Examiner has addressed Applicants arguments previously.

Applicants have stated that the Examiner asserts that the present disclosure fails to provide enablement of fragments and the one fragment present, GWIKQEEVDDIVQK, is not enabled for its use as a vaccine. Again, Applicants direct the Examiner to page 8, line 31 through page 9, line 2 and page 14, last paragraph where this issue is addressed. However, these portions of the specification (pages 8, 9 and 14) do not set forth enablement for the scope of the claimed invention.

"Applicants respectfully submit the publication by Schaap et al. (2004, Parasitology, vol. 128, 603-616). This journal article was published after the priority date of the application. Schaap et al. describes the cloning and the sequences of LDH's from the Eimeria species acervulina, tenella and maxima. The identity between the amino acid (aa) sequences is described as "rather low" and as "extensively diverged" being between 66 and 80% aa identity. A multiple alignment of the aa sequences is presented in figure 2 (p. 606). The aa sequence E. tenella LDH was used to model its 3D structure, which was compared to that of Plasmodium falciparum (Malaria) LDH. Remarkably, the E. tenella and P. falciparum LDH proteins share only 47% aa identity but have an almost identical 3 dimensional structure (see figure 3, page 609). The article asserts on page 609 (bottom of left column through top of right column): although the primary structure (the aa sequence) is "substantially different", their 3D structures are "very similar". Schaap et al. recite in the middle of that same page: "In summary... only shows 47% identity... conserved active site features... predicted to be a molecule with very similar properties."

"Therefore, Applicants respectfully submit the following as facts:

-the patent application shows effective vaccination with E. acervulina LDH

-the publication by Schaap et al. show aa sequences LDH protein of two more Eimeria species: tenella and maxima.

-these other two LDH proteins are "substantially different" in primary aa sequence: 66-80% identity.

-the 3D structure the tenella LDH was predicted by computer modeling, and was compared to that P. falciparum LDH

-the two 3D structures are "very similar"

-the primary aa sequence of the LDH proteins E. tenella and P. falciparum are only 47% identical.

From these submitted facts, Applicants respectfully submit the following logical conclusions:

1. When two LDH proteins being so dissimilar as E. tenella and falciparum (47% identity) are found to have a very conserved 3D structure, then the three Eimeria LDH's which are much more related the primary aa sequence level (66-80% identity) may be expected to be even more conserved in 3D structure.

2. It is common knowledge that a proteins 3D structure is important for immune-efficacy and the recognition of that protein by the immune system of a host-organism, consequently proteins with a highly similar 3D structure will also be similar in their immunogenic properties.

3. Consequently, as the E. acervulina LDH proved to be effective as a vaccine, therefore, the E. tenella and E. maxima LDH proteins, arguably having a 3D structure very similar to that of E. acervulina LDH, will also be effective in vaccines.

"Applicants respectfully submit that the biological variants of acervulina LDH, such as the E. tenella and E. maxima LDH proteins, will be equally effective vaccines as the E. acervulina LDH."

With regard to the above comments by Applicants, it is noted that these statements may be true, but they do not address the present rejection based on 112, scope of enablement of a vaccine that comprises a variant of the Eimeria LDH, not the complete Eimeria LDH protein. Please note that the Examiner views "variant" claim language in terms of the common definition of variant of a protein known in the art, i.e. amino acid substitutions, insertions or deletions. The same definition or meaning is given by Applicants in the specification, please see pages 7-8 of the specification.

With regard to Schaap et al, the Examiner agrees that the reference teaches that a 37 kD protein of Eimeria LDH was partially protective. This fact has never been a 112, first paragraph scope of enablement issue, but rather the enablement of a variant (i.e. amino acid substitutions, insertions or deletions) of this 37 kD

protein in a vaccine composition. Schaap et al does not address the use of a variant or part sequence or variant of the Eimeria LDH in a vaccine composition.

8. Claims 1-3, 11, 13, 16-20, 23, 24 and 26 are rejected under 35 U.S.C. 102(b) as being anticipated by Shirley, 1975, Parasitology, 71:369-376.

The claims are drawn to an isolated protein comprising one or more immunoreactive determinants of lactate dehydrogenase enzyme from *Eimeria acervulina*, immunogenic fragments and vaccines comprising the protein and immunogenic fragments in pharmaceutical carriers as well as a process for preparing a vaccine.

Shirley teaches lactate dehydrogenase enzyme from *E. acervulina*. The enzyme was prepared in NaCl solution (pharmaceutical carrier) and purified from sporozoites, oocysts and merozoites (pages 372, 373 and plate 1A). The protein of Shirley appears to be the same as the claimed protein. The formulation of the enzyme in NaCl meets the limitations of the claimed process. Characteristics such as immunoreactive determinants and amino acid seq. I.D. No. 2 would be inherent in the enzyme of the prior art. The recitation of "vaccine" is being viewed as intended use of the enzyme. Applicant's use of the open-ended term "comprising" in the claims fails to exclude unrecited steps and leaves the claims open for inclusion of unspecified ingredients, even in major amounts. See In re Horvitz, 168 F 2d 522, 78 U.S.P.Q. 79 (C.C.P.A. 1948) and Ex parte Davis et al., 80 U.S.P.Q. 448 (PTO d. App. 1948). Additionally, since the Office does not have the facilities for examining and comparing applicants' protein, vaccine and process with the protein, vaccine and process of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product, vaccine and process

and the product, vaccine and process of the prior art (i.e., that the protein, vaccine and process of the prior art does not possess the same material structural and functional characteristics of the claimed protein, vaccine and process). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

9. Claims 1-3, 16-18 and 23 are rejected under 35 U.S.C. 102(b) as being anticipated by Kucera, 1989, Folia Parasitologica 36/4:295-299.

The claims are drawn to an isolated protein comprising one or more immunoreactive determinants of lactate dehydrogenase enzyme from *Eimeria acervulina*, immunogenic fragments and vaccines comprising the protein and immunogenic fragments in pharmaceutical carriers as well as a process for preparing a vaccine.

Kucera teaches the lactate dehydrogenase enzyme from Eimeria acervulina and the isolation and purification of the enzyme (page 296, figure 3). The protein of Kucera appears to be the same as the claimed protein. Characteristics such as immunoreactive determinants and amino acid seq. I.D. No. 2 would be inherent in the enzyme of the prior art. The recitation of "vaccine" is being viewed as intended use of the enzyme. Applicant's use of the open-ended term "comprising" in the claims fails to exclude unrecited steps and leaves the claims open for inclusion of unspecified ingredients, even in major amounts. See In re Horvitz, 168 F 2d 522, 78 U.S.P.Q. 79 (C.C.P.A. 1948) and Ex parte Davis et al., 80 U.S.P.Q. 448 (PTO d. App. 1948). Additionally, since the Office does not have the facilities for examining and comparing applicants' protein, vaccine and process with the protein, vaccine and process of the prior art, the burden is on applicant to show a

novel or unobvious difference between the claimed product, vaccine and process and the product, vaccine and process of the prior art (i.e., that the protein, vaccine and process of the prior art does not possess the same material structural and functional characteristics of the claimed protein, vaccine and process). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

10. Claims 1-3, 16-18 and 23 are rejected under 35 U.S.C. 102(b) as being anticipated by Nakamura et al, 1991, Journal of Veterinary Medical Science, 53/6:1101-1103.

The claims are drawn to an isolated protein comprising one or more immunoreactive determinants of lactate dehydrogenase enzyme from Eimeria acervulina, immunogenic fragments and vaccines comprising the protein and immunogenic fragments in pharmaceutical carriers.

Nakamma et al teach the lactate dehydrogenase enzyme from Eimeria acervulina and the isolation and purification of the enzyme (figure 2, c, d, f). The protein of Nakamura et al appears to be the same as the claimed protein. Characteristics such as immunoreactive determinants and amino acid seq. I.D. No. 2 would be inherent in the enzyme of the prior art. The recitation of "vaccine" is being viewed as intended use of the enzyme. Applicant's use of the open-ended term "comprising" in the claims fails to exclude unrecited steps and leaves the claims open for inclusion of unspecified ingredients, even in major amounts. See In re Horvitz, 168 F 2d 522, 78 U.S.P.Q. 79 (C.C.P.A. 1948) and Ex parte Davis et al., 80 U.S.P.Q. 448 (PTO d. App. 1948). Additionally, since the Office does not have the facilities for examining and comparing applicants' protein, vaccine and

process with the protein, vaccine and process of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product, vaccine and process and the product, vaccine and process of the prior art (i.e., that the protein, vaccine and process of the prior art does not possess the same material structural and functional characteristics of the claimed protein, vaccine and process). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

11. With regard to the prior art rejections set forth in paragraphs 8-10, these rejections have been maintained for the reasons of record. Applicant's arguments filed November 25, 2003 have been fully considered but they are not persuasive. Applicants have asserted that the prior art (Shirley, Kucera et al, Nakamura et al) does not disclose or suggest the claimed invention of a protein expressed in vitro, comprising one or more immunoreactive and/or antigenic determinants of Eimeria lactate dehydrogenase (LDH), wherein said isolated protein is found intracellularly in Eimeria; a vaccine for the protection of poultry against Coccidiosis comprising an effective amount of an isolated protein comprising one or more immunoreactive and/or antigenic determinants of Eimeria lactate dehydrogenase, wherein said isolated protein is found intracellularly in Eimeria; and an immunogenic fragment of Eimeria lactate dehydrogenase (LDH), wherein said LDH is immunogenically reactive with antiserum raised against the polypeptide of SEQ ID NO:2. Applicants have asserted that the prior art, at best, discloses a native intact Eimeria LDH protein. Applicants have asserted that the prior art never mentions antigenic or immunogenic features nor does the prior art mention using these proteins as vaccines. Applicants completely disagree with Examiner's statement that the

recitation of "vaccine" is an intended use. The vaccine claims stand alone. A vaccine claim can be clearly patentable, if it is novel, even if the protein itself is anticipated. Applicants have asserted that the prior art fails to discuss a vaccine; thus, it is completely impossible for the prior art to anticipate a "vaccine" claim. "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, a single prior art reference." Verdegaal Bros. v. Union Oil Co. of California, 814 F.2d 628, 631, 2 U.S.P.Q.2d 1051/ 1053 (Fed. Cir. 1987). The prior art fails to disclose each element of the present invention as set forth in the claims.

With regard to Applicants' arguments, it is noted that "expressed in vitro" is viewed as a process limitation and does not negate the fact the prior art references disclose the Eimeria LDH. The antigenic or immunogenic features are inherent properties in the disclosed Eimeria. Determination of characteristics, which vary depending on the method of analysis, such as enzymatic activity, or other characteristics must be made by the same method under the same or analogous conditions to show differences that are not otherwise clearly apparent. With regard to Applicants' arguments concerning "vaccine", it is maintained that a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963).

With regard to the 102(b) anticipation art rejections set forth above, the rejections have been maintained for the reasons of record. Applicant's arguments filed July 29, 2004 have been fully considered but they are not persuasive. These arguments have been present previously and addressed by the Examiner.

12. The prior art rejections are maintained for the reasons of record. Applicant's arguments filed July 29, 2004 have been fully considered but they are not persuasive. It is noted that the Examiner has addressed the arguments previously.

13. No claims are allowed.

14. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to N. M. Minnifield whose telephone number is 571-272-0860. The examiner can normally be reached on M-F (8:00-5:30) Second Friday Off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette R.F. Smith can be reached on 571-272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

N. M. Minnifield
Primary Examiner
Art Unit 1645

NMM
September 2, 2004